Development of ROR1 CAR-T cells to target cancer stem cells in advanced malignancies

Grant Award Details

Development of ROR1 CAR-T cells to target cancer stem cells in advanced malignancies

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-10258

Project Objective: Conduct preclinical studies that will accelerate advancement of ROR1 CAR-T cell therapy toward first-in-human clinical studies.

Investigator:

Name:	Ezra Cohen
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Cancer

Human Stem Cell Use: Cancer Stem Cell

Cell Line Generation: Cancer Stem Cell

Award Value: $5,795,584

Status: Active

Grant Application Details

Application Title: Development of ROR1 CAR-T cells to target cancer stem cells in advanced malignancies

Public Abstract:

Translational Candidate

Autologous ROR1 CAR-T cell transduced with a lentiviral vector containing scFv (cirmtuzumab) with CD28, CD137, CD3zeta signaling domains

Area of Impact

ROR1 expressing cancer stem cells in solid tumors and hematologic tumors

Mechanism of Action

ROR1 CAR is a 3rd generation chimeric construct with an internal endodomain that transmits a CD3 zeta signal with added co-stimulatory signaling domains 4-1BB and CD28. When the transduced ROR-1 CAR-T cell comes into contact with its cognate receptor, a signal is transmitted by the CD3 zeta-chain, inducing lymphocyte proliferation and expression of trans-acting interleukins and chemokines that activate other immuno-reactive cells and in certain cases directly kill ROR1+ Cancer Stem Cells

Unmet Medical Need

Compelling evidence suggests that dormant cancer stem cells (CSCs) are considered the origin of therapeutic resistance, and are responsible for relapse and metastasis. We will selectively identify and attack CSCs through the ROR1 receptor, using CAR-T cells to address this unmet medical need.

Project Objective

Completion of a Pre-IND meeting

Major Proposed Activities

- Generate GMP-compatible ROR1 lentivirus with a single-chain variable fragment (scFv) with three signaling domains derived from CD3zeta, CD28 and 4-1BB
- Generate ROR1 CAR-T cells; complete studies of cell fate, persistence, efficacy and distribution in CLL, HNSCC, TNBC, ovarian, and pancreatic cancer
- Develop a ROR1 Companion Diagnostic test

Statement of Benefit to California:

Californians will benefit from this project in several significant ways. If the therapeutic is successful, it will extend the long-term survival rates for Californians with solid and hematologic tumors. Accomplishing the proposed studies will have an added economic benefit for California through creating and maintaining skilled jobs, and using resources from in-state companies. High cost hospital stays and treatments associated with advanced disease, will be significantly reduced.
